Clinical Update

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Diabetes mellitus and periodontal disease: a two-way street through health and disease

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Introduction

Diabetes Mellitus (DM) affects roughly 12 million people in the US; as many as half of these people may be unaware of their condition. Two forms of the disease exist. Type I DM (formerly Insulin Dependent Diabetes Mellitus) is a result of destruction of the Islet of Langerhan cells in the pancreas, resulting in a lack of endogenous insulin production. Type II DM (formerly Non-Insulin Dependent Diabetes Mellitus) comprises 85-90% of diabetes cases, and is a result of impaired insulin receptors on the target cells.[1] Periodontal disease includes a spectrum of plaque-induced, inflammatory conditions affecting gingiva, cementum, and alveolar bone. Estimates of the prevalence of gingivitis in the US range from 39-60%, while only 5-15% of the population suffers from severe generalized periodontitis.[2] The purpose of this clinical update is to present an evidence based review of the effects of diabetes on the clinical course of periodontal disease, as well as to argue the importance of achieving periodontal health in the overall management plan for both type I and type II diabetics.

Diagnosis and medical management of diabetes

The signs and symptoms of DM are the classic triad of polyuria, polydipsia, and polyphagia, together with pruritis, weakness, and fatigue. Physicians rely on a battery of tests to diagnose DM, including fasting blood glucose, oral glucose tolerance test, and casual plasma glucose (fasting not required). One particularly useful test to determine the level of metabolic control is the glycated hemoglobin A1c, or HbA1c. This measures the percentage of glycated hemoglobin moieties on red blood cells. The HbA1c gives a measure of the blood glucose status over the half-life of the RBC, which is about 30-90 days.[1] Metabolic control of DM involves special attention to diet, exercise, weight loss, and multiple pharmacologic agents. Type I diabetics require exogenous insulin. Type II diabetics are usually managed with the use of sulfonylureas such as glipizide or glyburide. These drugs stimulate insulin release from the pancreas, as well as promote insulin uptake in the tissues. Other drugs, such as metformin and troglitazone increase tissue sensitivity to insulin without increasing pancreatic release of insulin, minimizing the risk of a hypoglycemic crisis. Complications of DM are a direct result of hyperglycemia, and include retinopathy (DM is the leading cause of blindness in the US), nephropathy, neuropathy, macrovascular disease, and altered wound healing.[3]

The sixth complication of diabetes

Numerous cross-sectional and longitudinal studies have identified DM as a risk factor for periodontal diseases.[4-9] Ciancola et al.[4] looked at the periodontal condition of Type I diabetics, and compared them to non-diabetic controls. While the prevalence of periodontitis among non-diabetics aged 11-18 was only 1.7%, the same age range of diabetics had a prevalence of periodontitis of 9.8%. They also noted an almost linear increase of periodontitis with age, with 39% of subjects over 19 years old exhibiting mild to severe periodontitis. The progression of clinical attachment loss was found to be accelerated in Type I diabetics compared to non-diabetics in a study by Firalti.[8] The significant difference was noted despite similar levels of plaque control. Metabolic control of Type I DM has been shown to impact periodontal conditions. Safkan-Seppälä and Ainamo[6] demonstrated that poorly controlled Type I diabetics had significantly more clinical attachment loss and alveolar bone loss compared to those Type I diabetics with good glycemic control. The same association holds true for Type II diabetics. Emrich et al.[5] looked at the prevalence and severity of periodontal disease in Native Americans. Type II diabetics were found to have an increased risk of destructive periodontitis with an odds ratio ranging from 2.81 (based on clinical attachment loss) to 3.43 (based on alveolar bone loss.) Löe[7] found that 8% of non-diabetic Pima Indians under the age of 35 had advanced periodontal disease, versus 48% of Type II diabetics in the same age range. He estimated the diabetics were about three times more likely to exhibit periodontitis. In a longitudinal study, Taylor et al.[9] showed that Type II DM was associated with an increased rate of alveolar bone loss progression. Several mechanisms for worsened periodontal status in diabetics have been studied. Bissada et al[10] demonstrated both decreased chemotaxis and phagocytosis of PMNs in peripheral blood of diabetics. Derangements of collagen metabolism occur in diabetics. Golub et al.[11] showed *in vitro* and *in vivo* that collagenase activity is enhanced in diabetic rats. Also, a dose-dependent decrease in collagen production by fibroblasts was noted with increasing glucose concentrations.[12] In a hyperglycemic environment, numerous proteins, including collagen, undergo a non-enzymatic glycosylation process to form advanced glycation endproducts (AGEs). AGEs result in a myriad of events, including increased cross-linking and decreased solubility and turnover of collagen. AGEs induce macrophages and monocytes to increase secretion of pro-inflammatory cytokines such as interleukin-1 and tumor necrosis factor-α.[3] Zambon et al.[13] suggested that both quantitative and qualitative differences in periodontal pathogens could account for increased susceptibility to periodontitis in diabetics. Listgarten et al.[14] noted increased thickness of the basement membrane of capillary endothelium in diabetics compared to non-diabetics.

Periodontitis as a risk factor for diabetes

While it is well established that diabetes mellitus is a significant risk factor for periodontitis, researchers are beginning to look at the converse - periodontal infections negatively impacting the glycemic control of both Type I and Type II diabetics. As early as 1960, Williams and Mahan[15] noted a significant reduction in insulin requirements in 7 of 9 patients after periodontal therapy. Taylor et al.[16] in a seven year longitudinal study of Type II diabetics found that significantly more subjects demonstrated worsening glycemic

control who had severe periodontitis. Grossi et al.[17] in a randomized clinical trial of Type II diabetic Pima Indians showed that scaling and curettage plus systemic doxycycline was able to reduce HbA1c by almost 10%. More recently, Kuran et al.[18] noted an 11% decrease in HbA1c in Type II diabetics after oral hygiene instructions and full mouth scaling and root planing. Slight increases were noted in the control group, receiving only oral hygiene instructions. Both in vitro and animal studies have documented the role of the pro-inflammatory cytokine Tumor Necrosis Factor – α in insulin resistance. Iwamoto et al.[19] have shown that non-surgical periodontal therapy significantly reduced both HbA1c and serum TNF-α in thirteen Type II DM patients. They hypothesize that improved glycemic control is achieved by reduction of TNF-α and improved insulin resistance following control of periodontal inflammation. Taken together, the evidence suggests that control of periodontal disease should be an important part of the overall management of patients with DM.

Conclusion

The evidence overwhelmingly supports DM as a risk factor for periodontal disease. There is now a growing body of evidence that points to periodontal infections as an independent risk factor for poor glycemic control in patients with DM. With this knowledge, it is incumbent upon dentists and physicians alike to work together to achieve the desired goal of improvements in patient's overall health.

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